Atypical Paracaval Recurrence of Uterine Endometrial Stromal Sarcoma: A Case Report

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Abstract. Endometrial stromal sarcomas are rare uterine malignancies with a high capacity for recurrence, even in cases diagnosed at an early stage of the disease. Recurrence is usually confined to the pelvic space but sometimes accelerated growth and extension into the upper abdomen can be found. In such cases, an aggressive surgical approach might be needed in order to provide complete resection of the recurrent tumor. We present the case of a 51-year-old patient who was diagnosed with an atypical spindle-shaped recurrence stretching from the pelvic floor to the right renal hilum along the inferior vena cava following total interadnexial hysterectomy for a presumed benign uterine tumor. An R0 resection of the recurrent tumor was performed and the histopathological study revealed the presence of a low-grade endometrial stromal sarcoma.

Endometrial stromal sarcoma (ESS) is a rare uterine neoplasia, accounting for 1% of all uterine malignancies and 6-20% of uterine sarcomas, which originates from the endometrial stroma in its proliferative phase (1, 2). ESS were initially subdivided into low-grade and high-grade tumors, but according to the 2003 World Health Organization classification, the latter were considered as undifferentiated uterine sarcomas due to the fact that they exhibit destructive myometrial invasion rather than lymph node involvement (2-5). Low-grade ESS are characterized by slow growth, with a tendency to develop late recurrences, relapse occurring in up to 55% of cases, even in patients initially diagnosed with an early stage of the disease (1). Preoperatively, these tumors are often misdiagnosed due to their resemblance imaging to benign tumors, especially in younger women (6); in these cases, the suspicion of malignancy might be raised intraoperatively, and confirmed at the histopathological examination. We present the case of a 51-year-old patient diagnosed with a large paracaval recurrence who was previously submitted to surgery for a presumed benign uterine tumor in whom the histopathological findings revealed low-grade ESS.

Case Report

A 51-year-old patient diagnosed with an uterine tumor, in which the preoperative examinations suggested a uterine fibroma, was operated on the principles of benignity and a total interadnexial hysterectomy was performed. The histopathological examination revealed a low-grade ESS with tumor emboli in the vascular spaces. At one-year follow-up, computed tomography revealed a spindle-shaped recurrence stretching from the pelvic floor to the right renal hilum along the inferior cava vein. No distant metastases were identified. Intraoperatively, a large tumor adherent to the right iliac vessels, right ureter and inferior vena cava was found (Figure 1 and 2). The recurrent tumor was completely resected; pelvic and inter-aortico caval lymph node dissection were also performed (Figure 3). The left adnexa, which looked macroscopically normal, was also removed. The histopathological examination confirmed a low-grade recurrent ESS, measuring 11×5×3 cm. Immunohistochemistry revealed the diffuse presence of vimentin and CD10 in tumoral cells. Positivity for estrogen receptors was found in 85% of the tumor cells, while staining for Ki-67 was positive in 10% of the tumor cells. Neither the para-aortic lymph nodes nor the pelvic ones presented micro-metastasis. The postoperative course was uneventful; there were no signs of recurrent disease at the two-year follow-up.

Discussion

Most patients with ESS are diagnosed with an early stage of the disease, up to 86% of cases presenting uterine-confined malignancy (7); for these patients, total hysterectomy and

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peritoneal cavity exploration remain the therapeutic cornerstone (2). Due to the fact that ESS is a low-grade malignancy with an indolent course, ovarian-sparing surgery and even fertility-sparing surgery has been proposed by some authors (8, 9). The various reported outcomes and the fact that ESS remains a hormone-sensitive tumor are responsible for the fact that the efficacy and safety of this therapeutic strategy remain unclear (10).

There are authors who support the idea that an interadnexial hysterectomy should be taken into consideration, especially in young patients, with similar reported outcomes to those in whom surgical castration is performed (2, 7, 11). In their study, Chan et al. concluded that ovarian-sparing technique did not impact on survival in patients younger than 50 years with stage I-II disease (5-year overall survival rates of 96.2% versus 91.9%) (7). In contrast, there also exist studies which demonstrate the necessity of bilateral adnexectomy in order to prevent recurrence (12). For instance, Li et al. conducted a study on 53 patients with ESS; in 9 cases an interadnexial hysterectomy was performed, while in the other 44 cases, a total hysterectomy with bilateral adnexectomy was the treatment of choice. In all nine cases in which ovarian preservation was applied recurrence occurred, while in the other sub-group, recurrences were reported in only 10 out of the 44 cases ($p<0.001$) (12).

Several clinical and laboratory studies show that low-grade ESS are usually associated with hormone receptor positivity; due to this fact, adjuvant targeted-hormonal therapy should be taken into consideration in order to diminish the recurrence risk (13, 14).

When it comes to long-term outcomes, patients diagnosed with ESS have a high risk of developing peritoneal or pulmonary metastases (15) and also a high tendency for late...
local recurrences, with an estimated incidence of 36-56%, even for patients diagnosed with an early stage of the disease (2, 4-6, 13-15). However, ESS presents an indolent pattern of growth, with a reported median time-to-recurrence of 65 months for early stages and 9 months for patients who had initially been diagnosed with advanced-stage disease (15). Especially due to this indolent pattern of growth, cytoreductive surgery should be considered.

Regarding the role of lymph node dissection, matters are still debated. Although most studies could not conclude that the association of extended lymphadenectomy improves survival (5-year overall survival being 86% for node-positive cases versus 95% for node-negative cases according to Shah et al.’s series) (11), some other authors maintain that patients with positive lymph nodes have a significantly poorer survival (7). This conclusion was found especially in studies which evaluated the prognostic factors in groups of patients presenting a higher percentage of high-grade uterine sarcomas (7). In Chan et al.’s study, 831 patients diagnosed with ESS were included; in 282 of them, associated lymph node dissection was performed and positive lymph nodes were encountered in 9.9% of cases. The study concluded that lymph node involvement was a poor prognosis factor; however, the overall survival for patients submitted to lymph node dissection was not significantly different compared to those in whom lymphadenectomy had not been performed ($p=0.351$) (7).

Figure 2. Dissection of the right ureter and the right iliac vessels.
It is not well-established whether complete lymph node dissection should be performed or if limited resection of the enlarged lymph nodes is sufficient, and whether inter-aortico-caval lymph node dissection should be introduced as a routine surgical procedure. In order to provide a better standardized protocol, further prospective studies involving larger number of cases are still required (10).

When it comes to the mainstay of treatment in recurrent disease, surgery is widely accepted as the most effective therapeutic protocol in order to achieve a high cure rate. Surgery should be applied for pelvic, abdominal lymphatic, hepatic or even pulmonary recurrence (10, 16).

When studying the characteristics associated with improved outcome after surgery for recurrence, most studies conclude that a longer disease-free interval between primary diagnosis and surgery for first recurrence and complete resection of the recurrence represent the most important prognostic factors associated with an improved outcome (2). In the study of Ashraf et al., 14 patients diagnosed with ESS were included. After a median follow-up of 45.6 months, three patients had recurrences: in one case, recurrence developed at 9 months, while in the other two cases respectively recurrent disease was encountered at 6 and 8 years, respectively. The patient in whom recurrent disease was seen 9 months after initial surgery developed pelvic and lung metastases and was submitted to chemoradiation. The case in which a recurrence was diagnosed at the 6-year follow-up presented pelvic-confined disease and was submitted to surgery followed by adjuvant chemotherapy, while the last case was diagnosed with a vaginal and pulmonary recurrence and was submitted solely to chemotherapy. However none of the patients died from their disease. The 5-year overall survival rate for the entire cohort was 93%, while the median overall survival was 45.3 months (16). Prolonged survival after resection of recurrent tumors has also been reported in other studies (6, 12, 17). In the study conducted by Li et al., 53 patients with both low- and high-grade uterine ESS were included; 19 out of the 53 cases (35.8%) developed local or distant recurrences, with a median time to recurrence of 46 months. In 12 cases, local recurrences were diagnosed, seven cases experienced distant recurrence, while another two cases experienced both local and distant relapse. The median time to recurrence was significantly influenced by the histopathological subtype (61 months vs. 27 months for low-grade and high-grade sarcomas, respectively; \( p=0.003 \)). Other factors which influenced the development of recurrent disease were the presence of a high myometrial invasion (more than one-third of the myometrial depth) \( \left(p=0.006\right) \), ovarian preservation \( \left(p<0.001\right) \) and association...
of postoperative radiation therapy \((p=0.007)\). However, even among the cases diagnosed with stage I low-grade ESS, a recurrence rate of 25\% was seen. Once a recurrent tumor was diagnosed, surgery was the most common option for salvage therapy. In 11 cases, surgery was followed by adjuvant chemoradiation. Twelve out of the 19 patients survived longer than 3 years after the diagnosis of the first recurrence \((12)\).

Leath \textit{et al.} included 155 cases diagnosed with ESS from five institutions in their study; the main histopathological subtypes were low-grade ESS in 72 cases, high-grade ESS in 31 patients and unclassified lesions in two cases. At the time of initial surgery, bilateral salpingo-oophorectomy was undertaken in 64 cases diagnosed with low-grade ESS, in 26 cases with high-grade ESS and in both cases with unclassified histopathological subtypes. The authors reported a recurrence rate of 37\%, significantly higher in cases originating from high-grade ESS; the median time to recurrence was also shorter for cases with high-grade ESS (5 months vs. 55 months, \(p<0.0001\)) \((18)\).

In one of the largest and most homogenous cohorts involving ESS, Yoon \textit{et al.} included 117 patients diagnosed with low-grade ESS; recurrent disease was diagnosed in 33 patients. Recurrence rate by International Federation of Gynecology and Obstetrics (FIGO) stage was 26.1\% for stage I, 44.4\% for stage II, 50\% for stage III and 33.3\% for stage IV. Recurrent tumors were located in the pelvis alone in 51.5\% of cases, while extra-pelvic/pelvic disease was seen in 48.5\% of cases. The median overall survival after recurrent tumor resection was 133 months, while the 5-year overall survival rate after resection of the recurrence was 68.9\%. In univariate analysis, the most important positive prognostic factors for improved survival were initial FIGO stage I \((p=0.005)\), the presence of hormone receptors \((p=0.001)\) and complete resection of the recurrent tumor \((p=0.002)\), while initial ovarian preservation, lymph node dissection and site of recurrence did not have any significant association with post-recurrence survival. In multivariate analysis, the presence of hormone receptors and R0 resection of the recurrent lesion were independent positive prognostic factors after recurrence \((19)\).

Another common characteristic of ESS recurrence is tropism for vascular extension; thrombi usually form in ovarian or uterine vessels and exhibit an ascending development in the inferior cava vein, presenting even intracardiac extension. In these cases, more extensive surgical procedures might be needed involving resections and reconstructions of the great vessels \((20)\). In our case, at the time of surgery for recurrence, thrombi were located only at the level of the ovarian vessels, with no extension at the level of the inferior vena cava. An early diagnosis of recurrence gave us the opportunity to perform a curative resection without vascular resection, which might have increased the postoperative morbidity.

**Conclusion**

Women presenting with recurrent uterine sarcoma have an overall poor prognosis. However, due to the rarity of the disease and heterogeneity of most of the study groups which included patients with different disease stages and with different histopathological features, there is no obvious consensus regarding the standard therapeutic protocol which should be applied in recurrent ESS. However, in well-selected cases, debulking surgery seems to be the only way to control this aggressive malignancy, with good results in terms of survival.

**References**


